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REPORT M 043

SURFACE PARTICLE ANALYSIS OF GEL-FILLED MAMMARY IMPLANT

Mentor Corporation
Research & Development
201 Mentor Drive
Santa Barbara, CA 93111

July 26, 2004

ABSTRACT M 043

1.0 TITLE

SURFACE PARTICLE ANALYSIS OF GEL-FILLED MAMMARY IMPLANT

2.0 ABSTRACT

Particles on the surface of Mentor Gel-Filled Mammary Implants were analyzed to determine if free silica were present and to make a qualitative statement about the effectiveness of particulate removal by IPA washing. Optical microscopy and surface washing were performed by McCrone Associates, Inc. Test devices were smooth gel-filled 100 cc devices that represented sterilized, packaged finished product manufactured in Texas.

Gel mammary implants manufactured by Mentor Corporation are made largely from raw material from [redacted]. The implant is a flexible polysiloxane shell that contains gel filler. Amorphous fumed silica is formulated into the dip molding dispersion that comprises the device shell assembly. The dip molding dispersion is formulated at the vendor [redacted] not at Mentor Texas Operations. Device manufacturing entails shell dispersion dip molding and cure, shell cure, and shell assembly. The shell assembly is filled with gel formulation and cured. The Mentor manufacturing rooms are environmentally controlled to function as class 10000 clean rooms.

[redacted] conducted its surface particle analysis in a certified class 100 clean room to avoid the possibility of external particulate contamination. Class 100 specifies less than 100 particles that are 0.5 microns or larger, per cubic foot of atmosphere. Both a water wash an isopropyl alcohol (IPA) wash study were conducted. For each study duplicate devices were tested along with and a control sample that was intentionally dusted with silica provided by the raw material vendor, [redacted] Each device surface was microscopically examined for loose particulate before and after washing. The washing procedure was not intended to duplicate a manufacturing process nor was it intended to accomplish the complete removal of surface particles.

The surface area, utilized for the particle counting and measurement encompassed a circular area of approximately 1.3 sq in on the center of the anterior portion of each device. After the initial surface examination individual devices were briefly immersed (~30 s) in IPA or filtered water with gentle stirring. The individual respective solvent washes were filtered and the particles on the filter (22 mm diameter, 0.2 μm) were examined and counted. The washed devices were re-examined microscopically for particulate in the same area. Particle type, size and

number were reported as appropriate for the surface and filter analysis by microscopy.

Fibers and particles were observed on all the devices. None of the devices were observed to have the translucent particles characteristic of silica aggregates. After the washing process, all the device surfaces exhibited reduced numbers of particles and fibers.

Device surfaces that were intentionally dusted with silica were used to demonstrate that silica aggregates could be observed by microscopy on the device surface and on the filter. It was further demonstrated that both the water and the IPA washing procedure were effective in complete removal of silica.

2.0 AUTHOR

C. S. Puckett, Ph.D., Senior Scientist

Mentor Corporation
Research & Development
Santa Barbara, CA 93111

3.0 REFERENCES

1) Rebstock, Joseph, *Optical Microscopy Analysis of Implant Devices,* Project MA41350, [redacted], May 26, 2004.

2) Rebstock, Joseph, *Optical Microscopy Analysis of Implant Devices,* Project MA41591, [redacted], July 23, 2004.

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REPORT M 043

AQUEOUS WASH

[redacted]

26 May 2004

Catherine Puckett, Ph.D.
Mentor Corporation
201 Mentor Drive
Santa Barbara, CA 93111

Subject: Optical Microscopy Analysis of Implant Devices
Re: [redacted] Project MA41350

Dear Dr. Puckett:

This report summarizes our analysis of the above referenced project. The samples were received on 23 April 2004 and the analysis was performed under the authorization of your purchase order number 62287. Preliminary results were sent to you electronically by e-mail on 19 May 2004.

Introduction

The samples were three (3) gel-filled mammary implant devices from lot number 270022. Serial numbers (SN) for the three devices were: sample 1, TX1798736; sample 2, TX1798740; and sample 3, TX1798745. Full device descriptions and traceability information are provided in Appendix I of this report, which contains a copy of your protocol M043, and Appendix B – Table I. The samples were to be examined using an optical microscope for the presence of surface particulate following the procedure given in Protocol M043. The testing was being performed to determine if particles resembling aggregates of fumed silica were present on the samples, and could the fumed silica, if present, be distinguished from other particle types.

Samples 1 and 2 were duplicate samples for examination as received and after washing with water. The wash water was to be filtered and the filter membranes containing collected particles were to be examined.

Sample 3 was designed to be a positive control sample. This sample was to be initially examined as received, salted with particles from a bottle of amorphous fumed silica, which you provided with the samples, water washed and then re-examined along with a filter membrane prepared from the wash water.

All work performed on the samples was accomplished in our Class 100 clean-room facility. Representative photomicrographs were to be acquired of the particles observed on the samples >50 µm in size from each phase of the testing along with photomicrographs of the amorphous fumed silica that you provided.

Initial Examination of the Samples As Received

The samples were removed from the shipping containers and examined using a stereomicroscope at magnifications up to 90X using oblique lighting. When placed on the microscope stage with the top side up (curved side), a ring surrounding the information embossed on the back side was visible. The ring measured 3.3 cm in diameter and provided a known surface area of a known size for the analysis. The area within the ring equaled approximately one-eighth of the top surface. The samples were noted at this phase of the analysis as having a slightly tacky surface.

Particles present within the scanning area on the three (3) devices were described as colorless, irregular particles, and colorless fibers that resembled cellulosic fibers (paper or cotton). There were no particles observed that optically resembled aggregates of the fumed silica. A summary of the particles observed on each of the three (3) samples is contained in Table I. Optical photomicrographs acquired during the scanning are presented in Figures 1, 2, 5, 6, 9, 10 and 11.

Preparation of Sample 3, Positive Control

Following the initial examination, the device identified as sample 3 was lightly salted with amorphous fumed silica from the sample bottle that you provided. A dry #2 watercolor paint brush was dipped into the bottle and lightly tapped over the top surface of sample 3 producing numerous small particle aggregates. Representative images of the silica aggregates are presented in Figures 12, 13 and 14. Additional images of finely divided aggregates dispersed in immersion oil are presented in Figures 21 through 26.

Preparation and Analysis of Washed Samples

Prior to washing each sample, an internal procedure blank was prepared to verify the cleanliness of the particle-free water, the filtration system and the glassware to be used. An examination of the three (3) procedure blank filter membranes showed that no particles were being introduced by the water or the equipment.

Each implant device was placed in a beaker and immersed with ~250 mL of particle-free water for 30 seconds while stirring with a glass rod. Stirring was selected over sonication so that the silica aggregates added to sample 3 would not disassociate forming microscopic particulate. A surfactant was not added to

the water for the same reason. The method used was not anticipated to remove all particles from the devices due to the tackiness of the device surfaces.

The three (3) devices were removed from the beakers and placed in their original containers with the top side up and allowed to air dry before re-examining. The same top surface area as initially scanned was re-analyzed. Overall, the samples appeared to contain fewer particles. The particles observed within the known surface area were consistent with the initial particle types (colorless fibers and particles) at a similar or slightly lower frequency. There were no particles observed during this examination of the samples that resembled silica aggregates. A summary of the particles observed is contained in Table I. Optical photomicrographs acquired from the samples are presented in Figures 3, 7, 15 and 16.

Preparation and Analysis of the Filter Membranes

The wash water from the samples was filtered through 25 mm diameter, 0.2 µm polycarbonate filters. Each beaker was rinsed one time and the rinse solutions were filtered through the appropriate membranes.

The filters from the duplicate samples (samples 1 and 2) contained numerous, colorless particles and fibers similar to the particles previously observed plus a few colored fibers. Particles resembling silica aggregates were not observed on the duplicate samples.

The filter membrane from the positive control (sample 3) also contained colored and colorless fibers, and two types of colorless particles. One of the colorless particle types was consistent with the colorless particles previously observed. The second colorless particle type was slightly translucent with more of a gelatinous appearance. This second type of colorless particle was optically consistent with the amorphous fumed silica that was intentionally applied to the sample following the initial examination.

The results of the analysis are summarized in Table I. Optical photomicrographs acquired from the particles observed on the membranes are presented in Figures 4, 8, and 17 through 21.

Optical photomicrographs of a 1 mm stage micrometer used to calibrate the microscope ocular are presented in Figures 27 through 32. The images of the

stage micrometer can be used to approximate the size of particles visible in most of the Figure images.

Summary

None of the implant devices were found to contain particles that optically resembled silica aggregates, either during the initial inspection of the samples as received or after washing the samples in particle-free water. This includes the positive control sample (sample 3) that was deliberately salted with amorphous fumed silica, photographed and washed. Apparently, for these samples and the conditions used for the analysis, the washing process removed particulate that could be recognized as silica aggregates.

Likewise, the filter membranes from the wash water used for the duplicate samples (samples 1 and 2) produced no particles that resembled silica aggregates. The filter membrane from the positive control sample (sample 3) contained numerous translucent, colorless particles with a gelatinous appearance that were optically consistent with the amorphous fumed silica aggregates applied to this implant device.

Your samples are being returned to you with this report.

Thank you for consulting McCrone Associates. If you have any questions concerning this report, please do not hesitate to call.

Sincerely,

Joseph M. Rebstock
Senior Research Scientist

JMR/jc
Enclosures
Ref: MA41350; P.O. 62287

TABLE I

Summary of Results
Implant Devices 1, 2 & 3 (Control)

Sample	Examination	Colorless Particles		Colorless Fibers		Colored Fibers		
		# Observed	Size (µm)	# Observed	Length (µm)	# Observed	Length (µm)	Color(s)
1*	Device initial scan	11	50 - <100	1	335	0	---	---
		3	110, 157 & 167					
	Filter containing particles	Numerous	>100 - 400	Numerous	100 – > 1,000	12	100 – > 1,000	Red, black, blue, brown
	Device after washing	10	50 - ~185	4	450, 550 & 675	0	---	---
2*	Device initial scan	10	50 - <100	1	600	0	---	---
		2	150 & 184					
	Filter containing particles	Numerous	>100 - 150	Numerous	100 – > 1,000	6	100 – > 1,000	5-black & 1-blue
	Device after washing	5	50 - 133	4	160, 400, 660 & 2,500	0	---	---

* Note: Sample 1 serial # is TX1798736; Sample 2 serial # is TX1798740.

TABLE I - continued

Summary of Results
Implant Devices 1, 2 & 3 (Control)

Sample	Examination	Colorless/Translucent** Particles		Colorless Fibers		Colored Fibers		
		# Observed	Size (µm)	# Observed	Length (µm)	# Observed	Length (µm)	Color(s)
3* (Control)	Device initial scan	10	50 - 100	4	137, 150, 167 & 200	0	---	---
		2	250 & 400					
	Filter containing particles	Numerous	50 - 200	Numerous	100 – > 1,000	17	100 - >1,000	Red, pink, blue, black, yellow, brown
	Device after washing	4	50 – 150	3	460, 600 & 720	0	---	---
		3	185 - 540					

* Note: Sample 3 serial # is TX1798745

** Note: Translucent particles resembling silica aggregates were only observed on filter for sample 3.

Ref: MA41350

Figure 1. Representative stereomicroscope photomicrograph acquired from the top surface of sample 1 as received. Oblique illumination. Magnification = 44X. MA41350.

Figure 2. A second representative stereomicroscope photomicrograph acquired from the top surface of sample 1 as received. Oblique illumination. Magnification = 44X. MA41350.

Figure 3. Representative stereomicroscope photomicrograph acquired from the top surface of sample 1 after washing. Oblique illumination. Magnification = 44X. MA41350.

Figure 4. A representative stereomicroscope photomicrograph of particulate recovered from filtering the wash water from sample 1. Oblique illumination. Magnification = 44X. MA41350.

Figure 5. Representative stereomicroscope photomicrograph acquired from the top surface of sample 2 as received. Oblique illumination. Magnification = 22X. MA41350.

Figure 6. Representative stereomicroscope photomicrograph acquired from the top surface of sample 2 as received. Oblique illumination. Magnification = 44X. MA41350.

Figure 7. Representative stereomicroscope photomicrograph acquired from the top surface of sample 2 after washing. Oblique illumination. Magnification = 44X. MA41350.

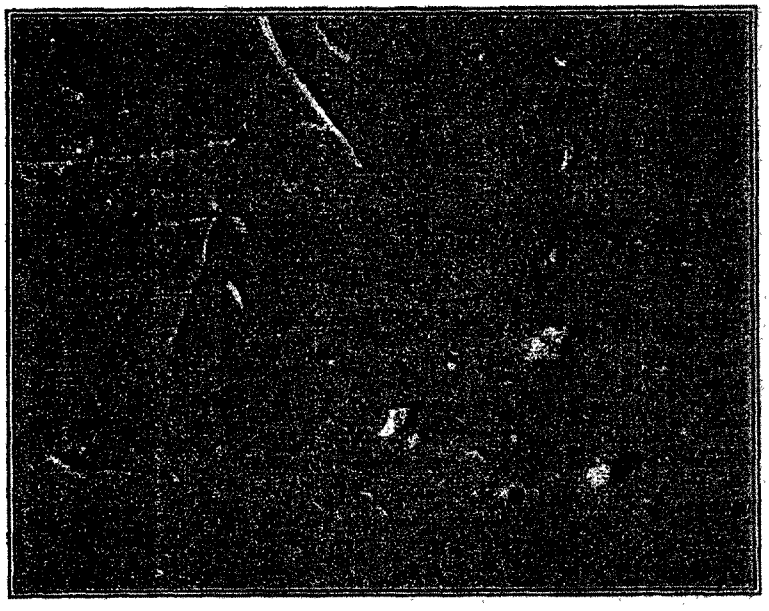

Figure 8. A representative stereomicroscope photomicrograph of particulate recovered from filtering the wash water from sample 2. Oblique illumination. Magnification = 44X. MA41350.

Figure 9. Representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) as received. Oblique illumination. Magnification = 44X. MA41350.

Figure 10. A second representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) as received. Oblique illumination. Magnification = 44X. MA41350.

Figure 11. Representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) as received. Oblique illumination. Magnification = 97X. MA41350.

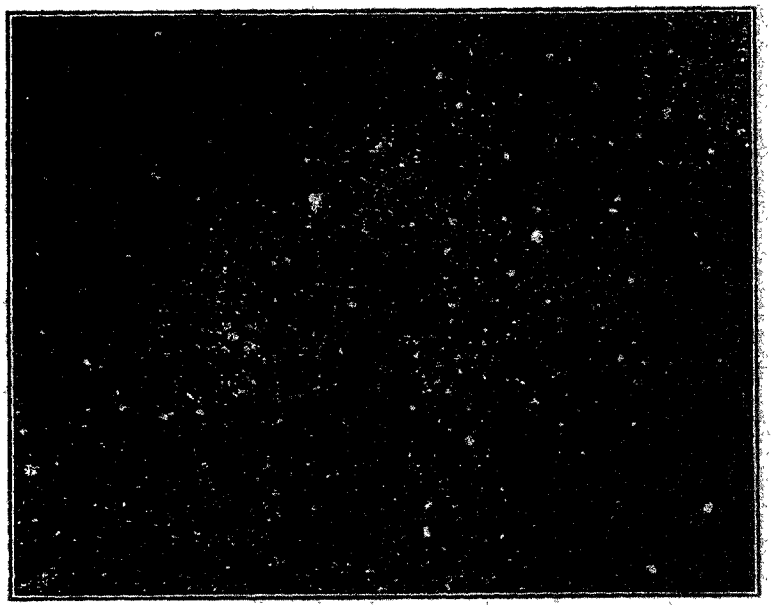

Figure 12. Representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) after adding silica particles. Oblique illumination. Magnification = 27X. MA41350.

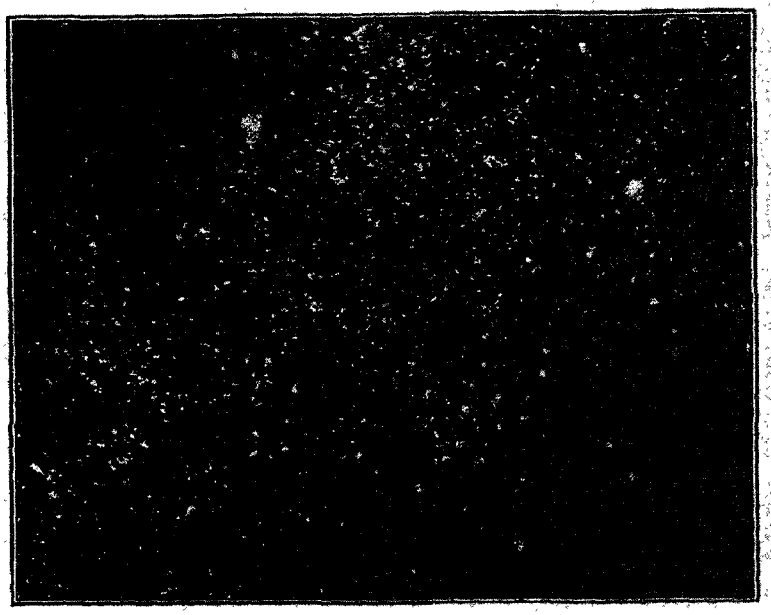

Figure 13. Representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) after adding silica particles. Oblique illumination. Magnification = 44X. MA41350.

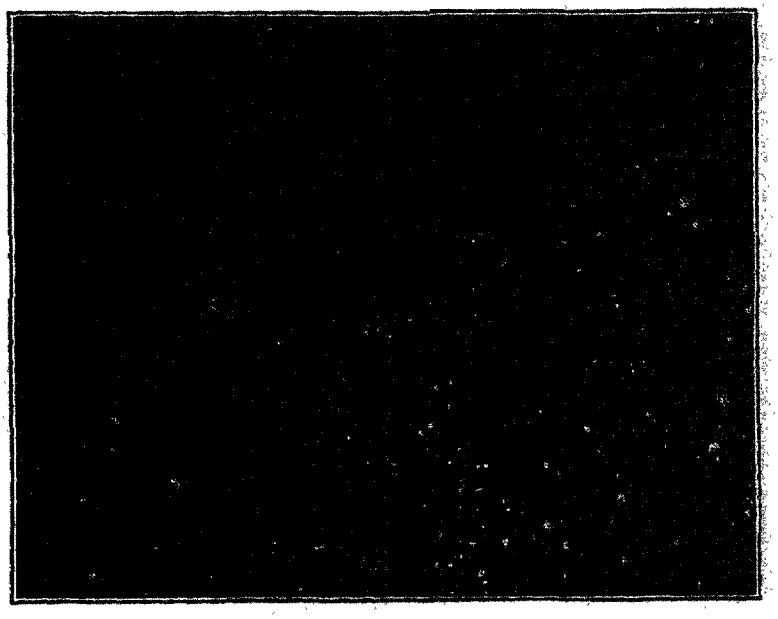

Figure 14. Representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) after adding silica particles. Oblique illumination. Magnification = 97X. MA41350.

Figure 15. Representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) after washing. Oblique illumination. Magnification = 27X. MA41350.

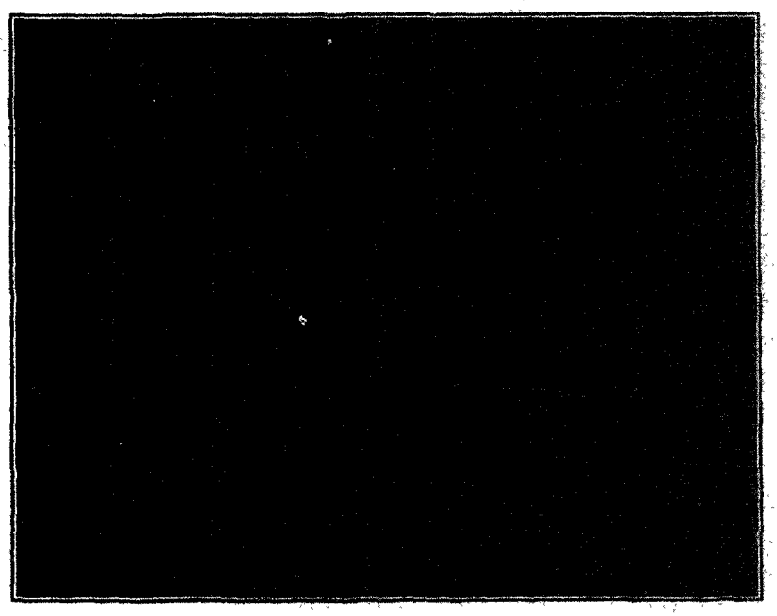

Figure 16. Representative stereomicroscope photomicrograph acquired from the top surface of sample 3 (positive control) after washing. Oblique illumination. Magnification = 44X. MA41350.

Figure 17. A representative stereomicroscope photomicrograph of particulate recovered from filtering the wash water from sample 3 (positive control). Oblique illumination. Magnification = 44X. MA41350.

Figure 18. A representative stereomicroscope photomicrograph of particulate recovered from filtering the wash water from sample 3 (positive control). Oblique illumination. Magnification = 55X. MA41350.

Figure 19. A representative stereomicroscope photomicrograph of particulate recovered from filtering the wash water from sample 3 (positive control). Oblique illumination. Magnification = 97X. MA41350.

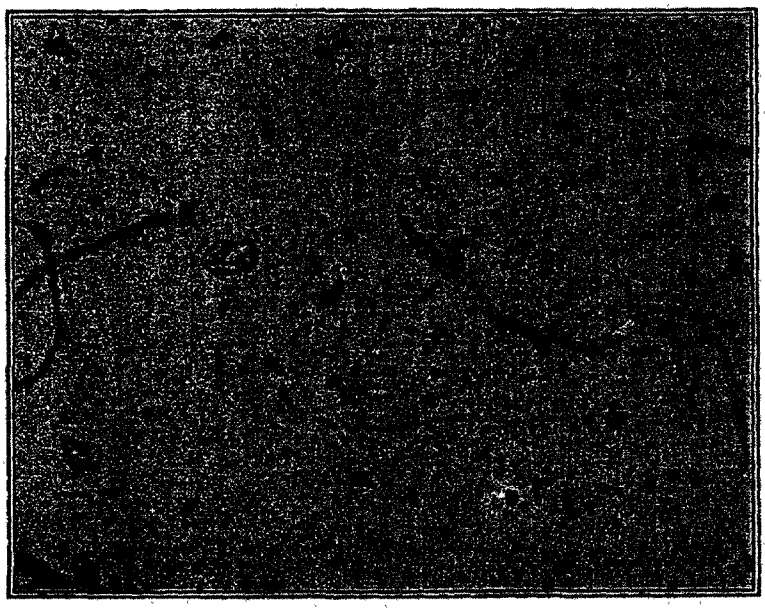

Figure 20. A representative stereomicroscope photomicrograph of particulate recovered from filtering the wash water from sample 3 (positive control). Epi illumination. Magnification = 97X. MA41350.

Figure 21. A representative stereomicroscope photomicrograph of amorphous fumed silica aggregates dispersed on a glass slide. Oblique illumination. Magnification = 44X. MA41350.

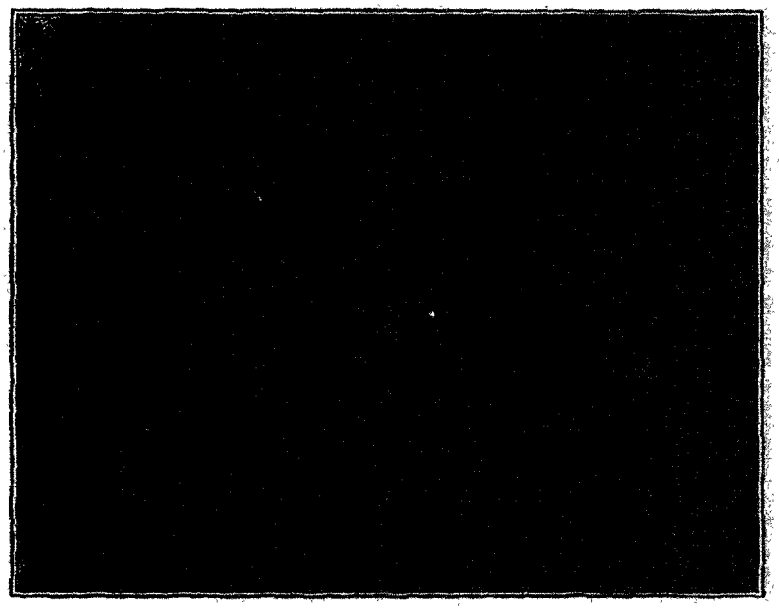

Figure 22. A representative stereomicroscope photomicrograph of amorphous fumed silica aggregates dispersed on a glass slide. Oblique illumination. Magnification = 97X. MA41350.

Figure 23. A representative polarizing light microscope photomicrograph of amorphous fumed silica aggregates dispersed on a glass slide in immersion oil beneath a cover slip. Transmitted light. Magnification = 150X. MA41350.

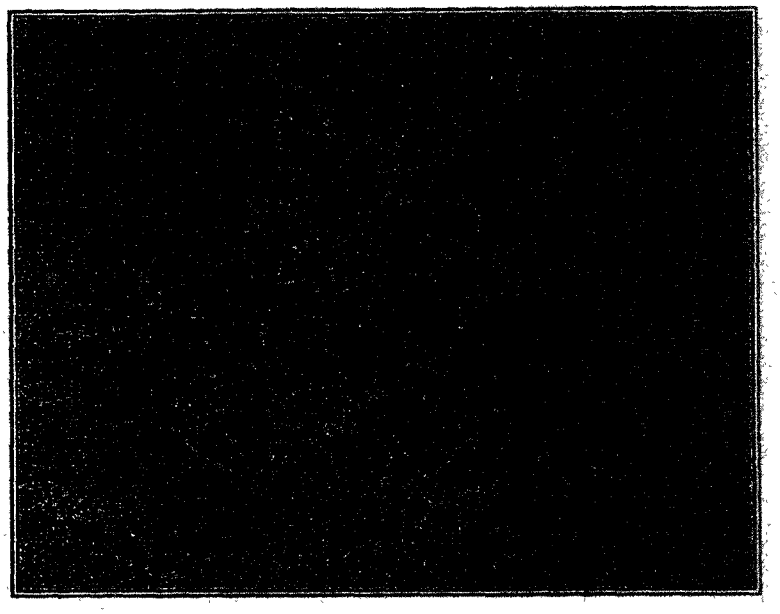

Figure 24. A representative polarizing light microscope photomicrograph of amorphous fumed silica aggregates dispersed on a glass slide in immersion oil beneath a cover slip. Transmitted light. Magnification = 300X. MA41350.

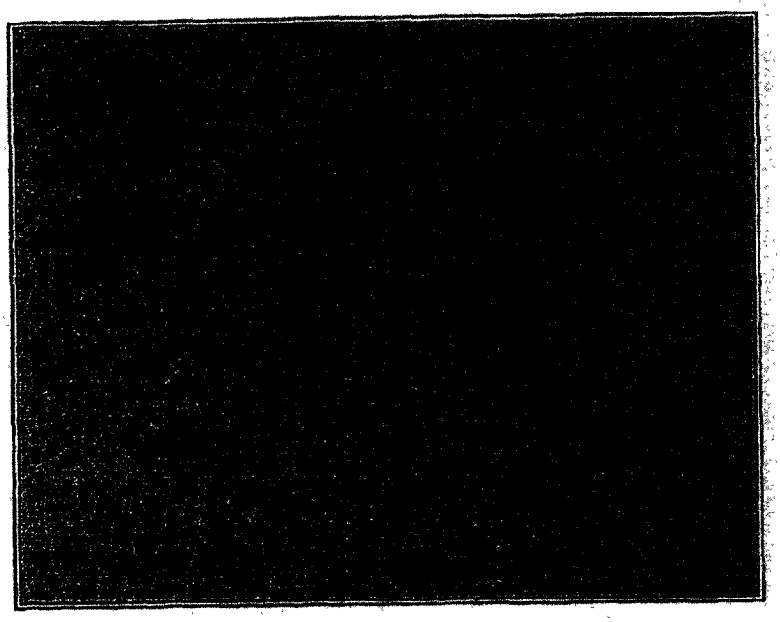

Figure 25. A representative polarizing light microscope photomicrograph of a second field-of-view of amorphous fumed silica aggregates dispersed on a glass slide in immersion oil beneath a cover slip. Transmitted light. Magnification = 150X. MA41350.

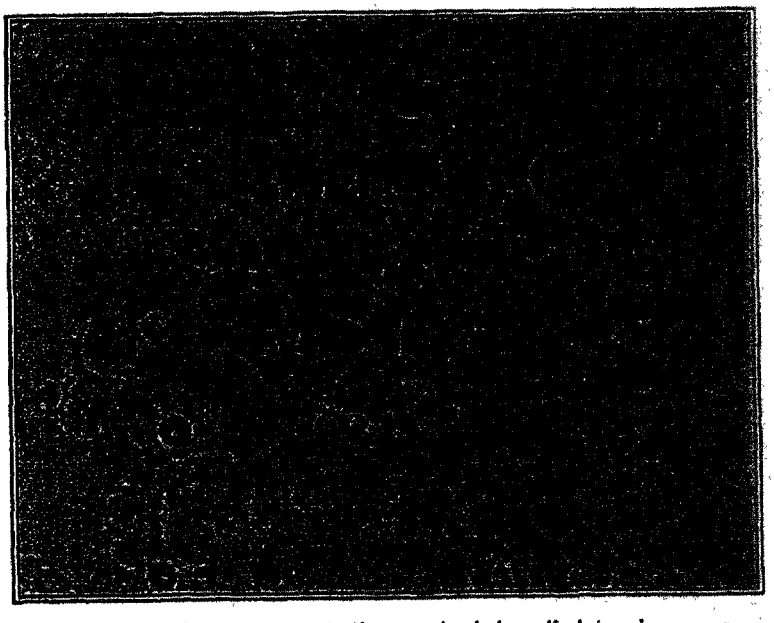

Figure 26. A representative polarizing light microscope photomicrograph of amorphous fumed silica aggregates dispersed on a glass slide in immersion oil beneath a cover slip. Transmitted light. Magnification = 300X. MA41350.

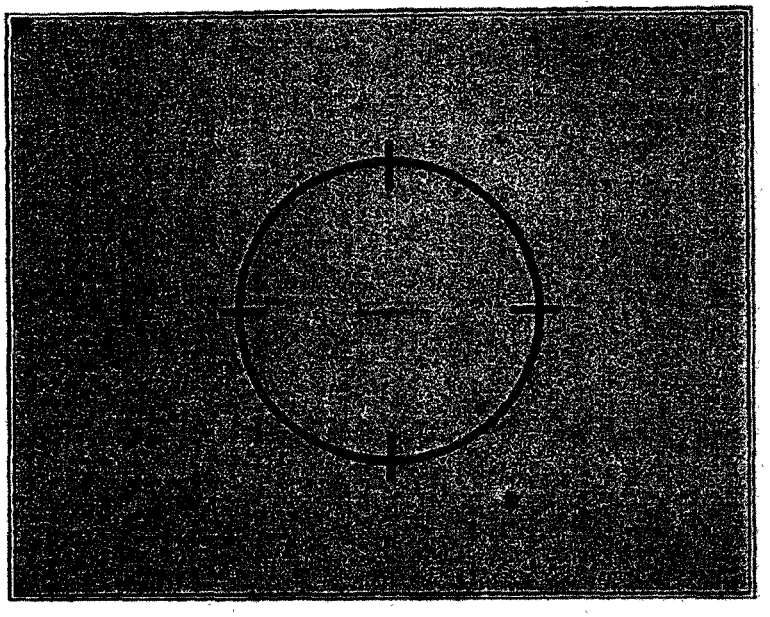

Figure 27. A stereomicroscope photomicrograph of a 1 mm stage micrometer. Transmitted light. Magnification = 11X. MA41350.

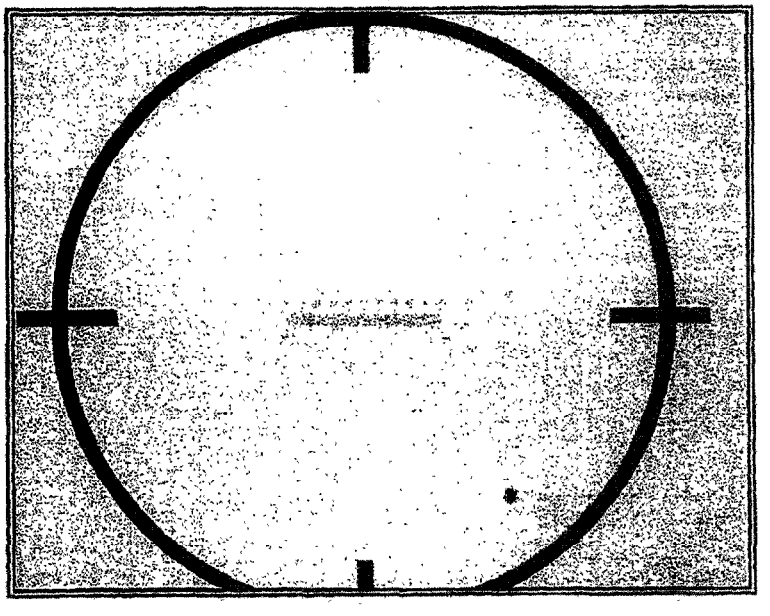

Figure 28. A stereomicroscope photomicrograph of a 1 mm stage micrometer. Transmitted light. Magnification = 22X. MA41350.

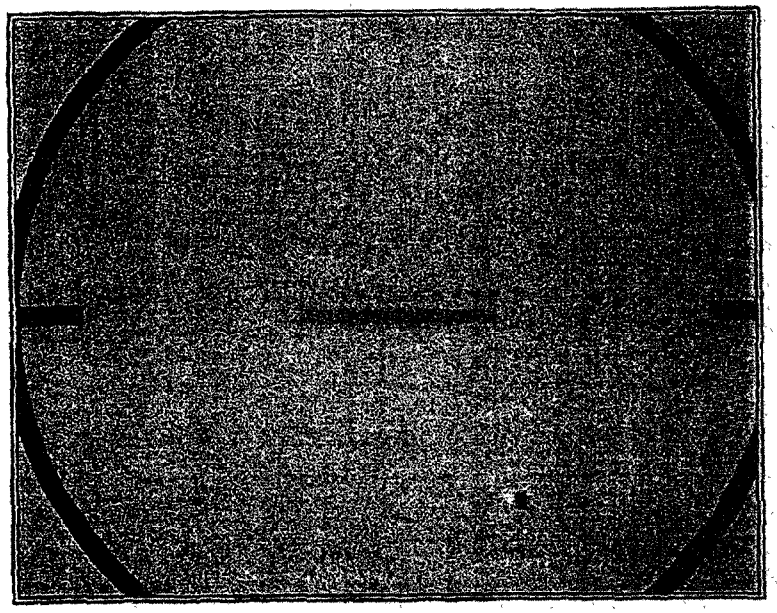

Figure 29. A stereomicroscope photomicrograph of a 1 mm stage micrometer. Transmitted light. Magnification = 27X. MA41350.

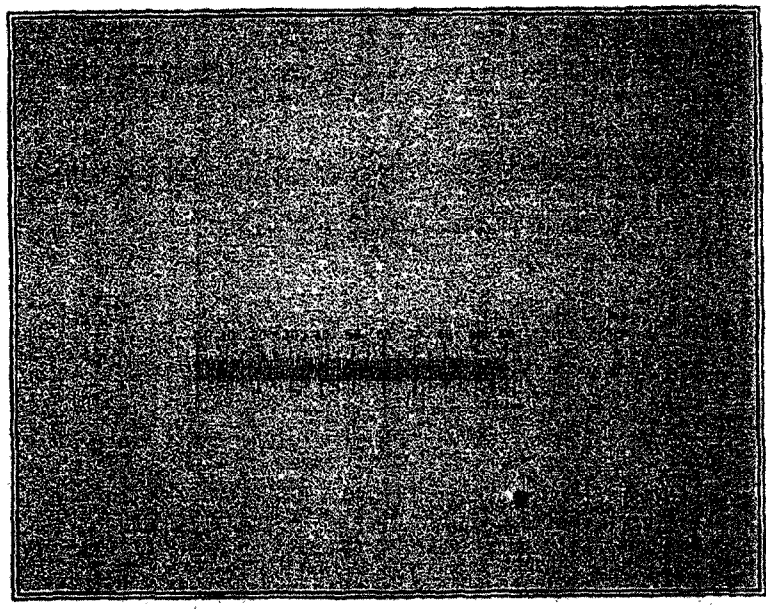

Figure 30. A stereomicroscope photomicrograph of a 1 mm stage micrometer. Transmitted light. Magnification = 44X. MA41350.

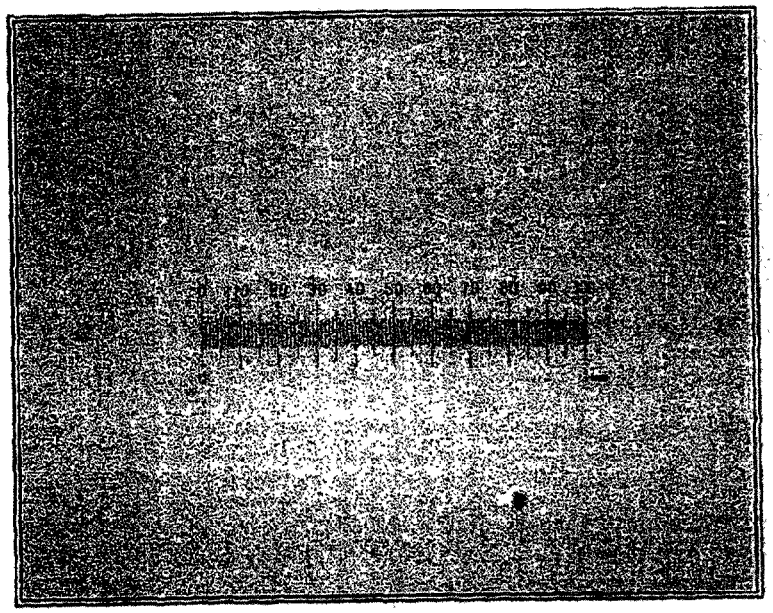

Figure 31. A stereomicroscope photomicrograph of a 1 mm stage micrometer. Transmitted light. Magnification = 55X. MA41350.

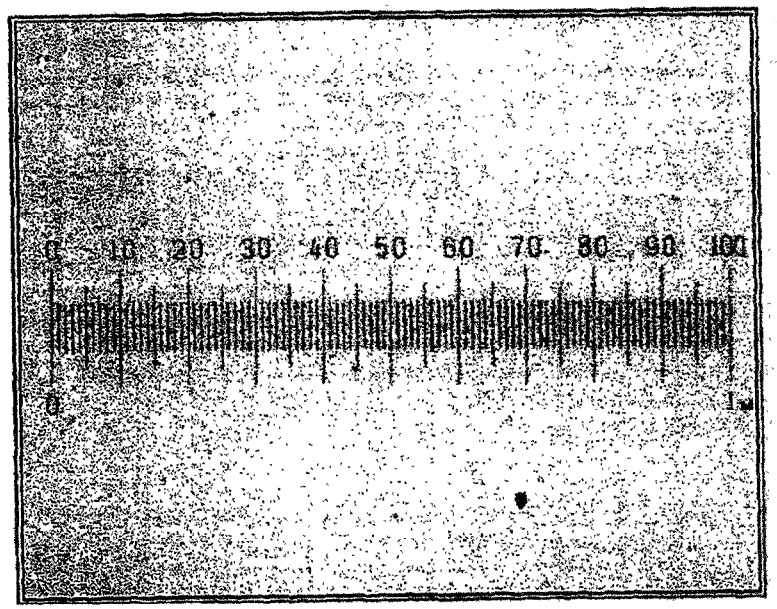

Figure 32. A stereomicroscope photomicrograph of a 1 mm stage micrometer. Transmitted light. Magnification = 97X. MA41350.